

**REMARKS**

Claims 1-22 are pending in this application. Claims 19-22 are canceled. Claims 1-19 have been rejected. Claims 1, 2, 7, 8, 13-15, and 18 have been amended and new claims 23-24 have been added. Please enter the amendments set forth above and the following remarks into the record.

**Restriction/Election Requirement**

Applicants elect Species I. Species I, claims 1-18, are elected without traverse for examination on the merits. Claims 20-22 have been canceled with Applicants reserving the right to file divisional or continuation applications on the methods of those claims.

**Rejection of Claims Under 35 U.S.C. 102(b)**

The Examiner has rejected claims 1-3, 10-14, 18, and 19 under 35 U.S.C. 102(b) as being anticipated by Schwarz, U.S. Patent No. 5026650 (hereinafter referred to as the ‘650 patent).

Applicants respectfully traverse the Examiner’s findings. Applicants would point out that invalidity for anticipation requires that there is no difference between the claimed invention and the reference disclosure as viewed by a person of ordinary skill in the field of the invention. See *Scripps Clinic and Research Foundation v. Genentech, Inc.*, 18 U.S.P.Q.2d 1001 (Fed. Cir. 1991).

**A. Independent Claim 1**

Amended claim 1 has a “chamber . . . containing circulating culture medium, wherein the membrane allows the flow of a set of biochemicals having a defined molecular weight between the growth compartment and the chamber.” In contrast, the ‘650 device does not have a chamber containing circulating culture medium. The ‘650 device has a “tubular oxygen permeable membrane 40” (column 5, lines 36-37) such as a silicone rubber membrane “which operates under air pressure to permit oxygen to permeate through the wall of the membrane into the annulus of the fluid medium surrounding the membrane and carbon dioxide to diffuse in the opposite direction.”

As stated by the Examiner, the bioreactor of the ‘650 patent is designed to facilitate the

movement of gases through the fluid inlet and outlet. The membrane 40 of the '650 device allows the passage of gas, not liquid medium. The membrane 40 is gas permeable, but is not liquid permeable. The '650 bioreactor would not work if liquid or media could penetrate the membrane 40. If media could penetrate membrane 40 the media would diffuse out of the bioreactor surrounding the membrane without being replenished. Thus, the '650 patent actually teaches away from the use of a liquid permeable molecular weight cut-off membrane.

A "fluid" is defined the American Heritage Dictionary as "a substance that exist, or is regarded as existing, as a continuum characterized by low resistance to flow and the tendency to assume the shape of its container." This definition encompasses both liquids and gases. A "liquid" is defined by the Concise Dictionary of Chemistry as "a phase of matter between that of a crystalline solid and a gas." The chamber of amended claim 1 contains "circulating culture medium." The '650 device does not have a chamber containing circulating culture medium. Similarly, the membrane 40 does not have defined pores that allow the flow of biochemicals having a defined molecular weight to pass through the pores. The membrane 40 of the '650 bioreactor is gas permeable, or allows diffusion of a pressurized gas. Gases are not considered biochemicals, which are principally considered to be proteins, carbohydrates, lipids, polynucleic acids, and the building blocks of those compounds.

Thus, the '650 patent does not anticipate the culture chamber of claim 1.

#### Claim 1's Dependent Claims

The culture chamber of amended claim 2 has a plurality of membrane carrier assemblies. The '650 bioreactor only has one membrane carrier assembly transversing the growth compartment.

Claims 10 and 11 involve a flexible (claim 10) molecular weight cut-off membrane having a molecular weight cut-off of about 100,000 daltons (claim 11). The '650 patent describes a gas permeable membrane, not a molecular weight cut-off membrane and certainly not a molecular weight cut-off membrane having very defined pores that would allow biochemicals having a molecular weight of about 100,000 daltons and less to pass through the membrane while restricting the passage of biochemicals having a molecular weight greater than 100,000 daltons.

Claims 13 and 14 regard a support cylinder having a number of radial cross holes extending to the exterior surface of the cylinder on each end of the cylinder. Figures 3 and 4 of the '650 patent clearly show that the support member 32 has only one opening 37 to the exterior surface of the support member at one end of the support member and only one opening 33 to the exterior surface of the support member at the opposite end of the support member.

In addition, claims 2-3 and 10-14 are dependent on amended claim 1. Each dependent claim contains all of the limitations of its independent claim. Thus, the dependent claims of independent claim are not anticipated by the '650 patent.

**B. Independent Claim 18**

Independent claim 18 is not anticipated by the '650 patent for the same reasons as set forth above for claim 1. In addition, the support cylinder of amended claim 18 has a number surface pockets in liquid communication with the through bore of the end fitting of the housing. The support cylinder 32 of the '650 patent does not have surface pockets or a plurality of coplanar radial cross holes intersecting those surface pockets.

Thus, the '650 patent does not anticipate the culture chamber of claim 18.

**C. Independent Claim 19**

Independent claim 19 has been canceled.

**Rejection of Claims Under 35 U.S.C. 103(a)**

**A. Regarding Schwartz (U.S. 5155035) in view of Bauer (U.S. 6107055)**

The Examiner has rejected claims 1, 2, 7, 8 and 10-12 under 35 U.S.C. 103(a) as being unpatentable over Schwartz (U.S. 5155035, hereinafter the '035 patent) in view of Bauer (U.S. 6107055, hereinafter the '055 patent). Applicants traverse the rejection for the reasons discussed below.

The culture chamber of independent claim 1 has a membrane carrier assembly that is distinctly different from the filtering unit of the '035 patent and the '055 patent. The filter assembly 35 of the '035 patent does not have a support cylinder that transverses the growth compartment.

Likewise, the filter assembly 35 does not have a molecular weight cut-off membrane. Furthermore, the filter assembly does not have a chamber bordered on one side by the exterior surface of the cylinder and on an opposed side by an interior surface of the membrane.

Similarly, the Bauer device described in the '055 patent does not have a membrane carrier device like that of claim 1. The '055 bioreactor does not have a support cylinder transversing the growth compartment. The '055 bioreactor does use molecular weight cut-off membranes, but it uses the membranes in a different way and in a very different device. The '055 device does not have a chamber bordered on one side by the exterior surface of the cylinder and on an opposed side by an interior surface of the membrane. The Bauer device is a non-cellular device that moves biochemicals from one chamber to another chamber by pressurizing the chamber to force the biochemicals across the membrane between the two chambers. The present invention uses diffusion from the circulating medium down a concentration gradient, rather than using pressure to transport biochemicals across the membrane.

To establish a prima facie case of obviousness, the prior art must teach or suggest all claim limitations. In this case, neither the '035 patent or the '055 patent teach a support cylinder transversing the growth chamber. Nor does either patent teach a chamber bounded by and between the exterior surface of the cylinder and an interior surface of the membrane.

Claims 2, 7, 8 and 10-12 are dependent on amended claim 1. Each dependent claim contains all of the limitations of its independent claim. Thus, the dependent claims of independent claim 1 are patentably distinct from the '035 and the '055 patents.

B. Regarding Schwartz (U.S. 5155035) in view of Bauer (U.S. 6107055) and further in view of Schwartz (US 5026650)

The Examiner has rejected claims 3-6, 18 and 19 under 35 U.S.C. 103(a) as being unpatentable over Schwartz (U.S. 5155035, hereinafter the '035 patent) in view of Bauer (U.S. 6107055, hereinafter the '055 patent) and further in view of Schwartz (US 5026650, hereinafter the '650 patent). Applicants traverse the rejection for the reasons discussed below.

(1) Independent Claim 1

Independent claim 1 is discussed first, since claims 3-6 are dependent on claim 1 and include all of the limitations of claim 1. The membrane carrier assembly of claim 1 is distinct from the filtering units of the Schwartz '035 patent in that the filter assembly 35 does not have a support cylinder that transverses the growth compartment and does not have a molecular weight cut-off membrane as discussed above. Furthermore, the '035 patent describes the separate rotation of the chamber, the output shaft and filter arm, and the input shaft and the blade system. The present invention does not use a rotating filter or blade system. The '035 patent describes the use of the rotation of the components to create a transient shear stress in the growth compartment to clear the surface of the central tubular filter. In contrast, the chamber of the present invention between the exterior surface of the cylinder and interior surface of the membrane was designed to specifically allow for the circulation of fluid medium through the growth chamber without subjecting the cells within the growth compartment to shear stress.

Likewise, as discussed above, the Bauer '055 patent does not have a support cylinder that transverses the growth compartment, nor does the '055 patent have a chamber containing circulating culture medium that is bordered on one side by an exterior surface of the support cylinder and on an opposed side by a molecular weight cut-off membrane. Again the Bauer '055 device was designed to serve contrasting functions. The '055 bioreactor was designed as a non-cellular bioreactor. The principles desired and optimized for non-cellular reactors are very different from those desired for cell culture devices.

The Schwartz '650 patent teaches a support member 32 with a gas permeable membrane 40. As discussed above the '650 patent does not teach a liquid circulation system for circulating medium through the growth compartment, molecular weight cut-off membrane, or a chamber containing circulating culture medium. In fact if liquid could penetrate membrane 40 the media would diffuse out of the bioreactor without being replenished. Thus, the '650 patent actually teaches away from the use of a liquid permeable molecular weight cut-off membrane.

In contrast to the static bioreactor described in the '650 patent, the device of the present invention uses a liquid circulation system between the exterior surface of the support cylinder and the interior of the membrane to enhance diffusion of biochemicals into and out of the growth compartment. The basic concepts of gas permeability and biochemical diffusion down a

concentration gradient are significantly different and a device designed to aid in gas permeability across a membrane would not be considered a model for designing a chamber to encourage molecular diffusion down a concentration gradient.

A person with ordinary skill in the art of cell culture is technically skilled and generally has a Bachelor of Science degree. Typically, a person skilled in the art that cultures cells is concerned about maintaining viable and healthy cells and will not consider changing conditions that are likely to compromise the viability of the growing cells. The Schwartz '650 device is used for static cultures and the gas permeable membrane is used primarily to provide the culture with continuous oxygenation. The design of devices for gas permeability would not be used by one skilled in the art as a basis for designing a biochemical diffusion chamber using a circulating liquid medium.

Thus, each of the devices cited are designed to address and solve different problems with different types of reactors. The device design to address these different functions would be considered contradictory to the optimization of a cell culture device to address the problems described in the present application. Thus, Applicants suggest that a technician skilled in the art of growing cells would not combine the various aspects of the '035 patented device, the '055 patented device, and the '650 patented device to arrive at the current invention.

(2) Independent Claim 18

Applicants submit that Claim 18 is patentably distinct from the teachings of the '035 patent, the '055 patent and the '650 patent for all of the reasons cited above. In addition, Claim 18 claims a liquid channel on each end of the support cylinder, where each liquid channel has a plurality of surface pockets intersected by the coplanar radial cross holes and where the liquid channels are in liquid communication with the through bores of the end fittings and the growth compartment.

None of the three cited patents have a similar liquid channel having surface pockets on a support cylinder transversing the growth chamber, or a plurality of coplanar radial cross holes that intersect the surface pockets.

C. Regarding Schwartz (U.S. 5026650) in view of Kersten (U.S. 628607)

The Examiner has rejected claims 13-17 under 35 U.S.C. 103(a) as being unpatentable over

Schwartz (U.S. 5026650, hereinafter the '650 patent) as applied to claim 14, and further in view of Kersten (U.S. 628607, hereinafter the '607 patent). Applicants traverse the rejection for the reasons discussed below.

Amended claim 13 regards a support cylinder having a number of radial cross holes extending to the exterior surface of the cylinder on each end of the cylinder. Figures 3 and 4 of the '650 patent clearly show that the support member 32 has only one opening 37 to the exterior surface of the support member at one end of the support member and only one opening 33 to the exterior surface of the support member at the opposite end of the support member. Furthermore, amended claim 14 recites the radial holes of claim 13 are coplanar and equispaced about the exterior surface of the cylinder. Claims 15-17 regard surface pockets on the exterior surface of the cylinder.

The single opening 33 and 37 on each end of the support member of the '650 patent is not the same as a plurality of coplanar radial cross holes. The cited '650 patent describes a chamber made with a gas permeable membrane and a support member where the gas enters through one opening on one end and leaves through one opening on the other end. The flow and permeability of gas is distinctly different than the flow and permeability of liquids. The current invention uses the multiple radial cross holes to evenly distribute the circulating fluid through the liquid circulation system. A single cross hole would create pressure on one side of the membrane and is not optimum for enhancing the diffusion of biochemicals through the membrane.

The unique design of the coplanar, equispaced cross holes intersecting arcuate surface pockets has basically been dismissed by the Examiner. Neither the Schwartz '650 patent nor the Kersten '607 patent describe or consider radial coplanar cross holes intersecting surface pockets. Applicants submit that the surface pockets are uniquely designed "to produce a sufficient pressure area so that the elastic resistance of membrane 37 can be overcome" (see paragraph 48). The flow of gas in the '650 device does not require overcoming the resistance of the membrane as described for the present invention.

The grooves 204 transversing the spacer 201 as described in the Kersten '607 patent are not arcuate surface pockets, nor are they intersected by coplanar radial cross holes. The grooves 204 are just that "grooves" on the surface of the spacer to assist in distributing gas and fluids along a

portion of the surface of a membrane. The grooves do not intercommunicate with each other to form a chamber enclosed between the exterior surface of a cylinder and the interior surface of a membrane.

**Terminal Disclaimer**

A Terminal Disclaimer is attached hereto following page 14.

**Conclusion**


In view of the foregoing amendments and remarks, it is respectfully submitted that Applicants have responded in a fully satisfactory manner to all matters at issue in this Office Action.

If the Examiner has any questions or suggestions concerning the application, or feels that an interview would advance the examination process, the Examiner is requested to call the Applicants' undersigned attorney at the direct dial number printed below.

Respectfully submitted,

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